

Research Article

An efficient procedure for the synthesis of ^{18}O -labelled methanesulfinyl chloride

Józef Drabowicz, Bogdan Bujnicki and Marian Mikolajczyk*
*Center of Molecular and Macromolecular Studies, Polish Academy of Sciences,
Department of Heteroorganic Chemistry, 90-363 Łódź, Sienkiewicza 112,
Poland*

Summary

A new procedure for the synthesis of methanesulfinyl chloride is described which involves chlorination of dimethyl disulfide with sulfuryl chloride in the presence of hexamethyldisiloxane. The use of ^{18}O -labelled hexamethyldisiloxane in this reaction results in the formation of ^{18}O -labelled methanesulfinyl chloride. Copyright © 2003 John Wiley & Sons, Ltd.

Key Words: oxygen-18; methanesulfinyl chloride; hexamethyldisiloxane; dimethyl disulfide; oxidative chlorination

Introduction

Sulfinyl chlorides are commonly used as substrates for the preparation of racemic and optically active sulfinyl derivatives such as sulfinates, thiosulfinates, sulfinamides and sulfoxides.¹ Among various sulfinyl chlorides, methanesulfinyl chloride **1**, the parent member of the aliphatic chloride family, plays a key role. This is due to the fact that starting from this chloride one can prepare a series of racemic alkyl methyl and aryl methyl sulfoxides as well as their optically active analogues. The latter have been very often applied as key substrates for

*Correspondence to: M. Mikolajczyk, Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Heteroorganic Chemistry, 90-363 Łódź, Sienkiewicza 112, Poland. E-mail: marmikol@bilbo.cbmm.lodz.pl

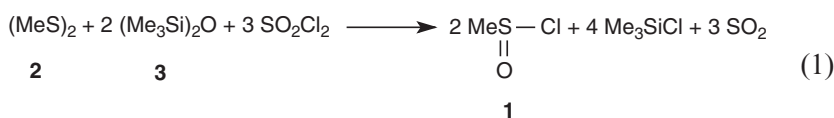
the asymmetric carbon–carbon or carbon–heteroatom bond formation.² Moreover, methyl aryl sulfoxides labelled with oxygen ¹⁸O have been frequently used as model compounds in many mechanistic studies.³ Therefore, it is obvious that an easy access to methanesulfinyl chloride **1** labelled with ¹⁸O-isotope should allow convenient and efficient preparation of ¹⁸O-labelled methyl sulfoxides and other sulfinyl derivatives.

Although in the chemical literature one can find a few useful procedures for the preparation of non-labelled methanesulfinyl chloride **1**,⁴ there is no protocol which describes an effective synthesis of this chloride labelled with the ¹⁸O-isotope. In this context, it is of interest to note that the procedures used for the preparation of ¹⁸O-arenesulfinyl chlorides, involving the reaction of labelled arenesulfinic acids with thionyl chloride,⁵ are less suitable for the synthesis of ¹⁸O-**1**, owing to the physico-chemical properties of this chloride and its precursor methanesulfinic acid.

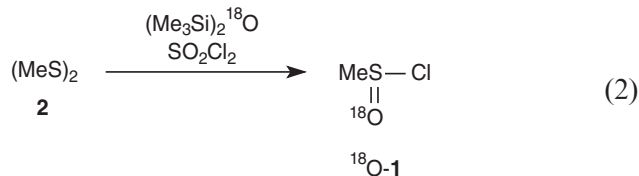
Results and discussion

In a previous study we developed the preparation of sulfinyl chlorides through the oxidative chlorination of sulfenyl derivatives with the trimethylsilyl acetate/sulfuryl chloride system.⁶ Moreover, we found that hexamethyldisiloxane acts as the chloride anion acceptor in the reaction of sulfinyl chlorides with chlorosulfites.⁷ As a continuation of these studies, we wish to disclose herein a new method for the synthesis of methanesulfinyl chloride **1** which is best suitable for the preparation of its ¹⁸O-analogue. It consists of the treatment of dimethyl disulfide **2** with sulfuryl chloride in the presence of hexamethyldisiloxane **3** or its ¹⁸O-analogue. In the case of a large scale preparation the trimethylchlorosilane formed can be reused for the preparation of hexamethyldisiloxane. Hexamethyldisiloxane **3** serves in this reaction as the oxygen donor and chloride anion acceptor. The conversion of dimethyl disulfide **2** into methanesulfinyl chloride **1** (Equation (1)), occurs at temperatures between –10°C and 25°C in less than 1 h after addition of sulfuryl chloride to a mixture of dimethyl disulfide **2** and hexamethyldisiloxane **3**. The yield of the crude product is quantitative (¹H-NMR assay) and the pure sulfinyl chloride is isolated in >90% yield by simple distillation of the residue after removal of the highly volatile trimethylchlorosilane. This procedure has

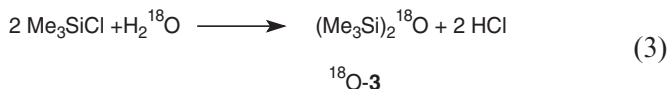
already been patented.⁸



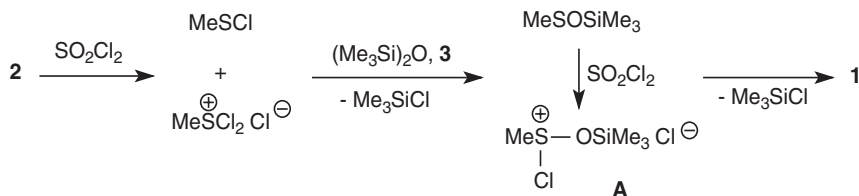
When ¹⁸O-labelled hexamethyldisiloxane **3** was used in this reaction, ¹⁸O-labelled methanesulfinyl chloride ¹⁸O-**1**, was obtained in 70% yield and with 92.5% ¹⁸O-content (MS assay) (Equation (2)).



The required ¹⁸O-**3** was easily prepared in the reaction of trimethylchlorosilane and ¹⁸O-water (Equation (3)).



Although the mechanistic details of the reaction under discussion were not investigated, almost full transfer of ¹⁸O-isotope from hexamethyldisiloxane **3** to sulfur may be most reasonably explained by the sequence of events depicted in Scheme 1.



Scheme 1.

In the first step, dimethyl disulfide **2** undergoes chlorination with sulfuryl chloride to methanesulfinyl chloride and/or to methyldichlorosulfonium chloride as an exhaustive chlorination product. Methanesulfinyl chloride reacts then with hexamethyldisiloxane **3** to give trimethylsilyl methanesulfenate which upon treatment with sulfuryl chloride forms the sulfonium salt **A** as a key intermediate. This salt may

be directly formed from methyldichlorosulfonium chloride and **3**. In the final step, elimination of trimethylsilyl chloride from **A** gives methanesulfinyl chloride **1**.

In our attempts to extend the above procedure to the preparation of aliphatic sulfinyl chlorides containing longer carbon chains we have noted that in the reaction of diethyl and di-*n*-propyl disulfides with sulfuryl chloride in the presence of hexamethyldisiloxane the corresponding sulfinyl chlorides were also formed as the main reaction products (¹H-NMR analysis of the crude reaction products). However, due to the presence of many sulfur containing by-products their complete purification by distillation could not be achieved.

Experimental

Methanesulfinyl chloride 1

To a mixture of dimethyl disulfide **2** (4.7 g, 0.05 mol) and hexamethyldisiloxane **3** (16.2 g, 0.1 mol) cooled to -10°C , sulfuryl chloride (20.5 g, 0.15 mol) was added dropwise with stirring over a course of 30 min. After completing the addition, the reaction mixture was allowed to reach room temperature over 45 min. After removal of the last traces of sulfur dioxide and the whole of the trimethylchlorosilane below room temperature, the residue was distilled on a water pump to give pure chloride **1**: yield 9 g (92%); b.p. $58\text{--}60^{\circ}\text{C}/26\text{ mmHg}$; Lit.^{4d} b.p. $55^{\circ}\text{C}/40\text{ mmHg}$; ¹H-NMR (CDCl_3) $\delta = 3.37$ (s).

¹⁸O-hexamethyldisiloxane ¹⁸O-3

A round-bottom flask protected from moisture by a standard calcium chloride tube was charged with ¹⁸O-water (0.55 g, 0.03 mol; ¹⁸O-content 24.1%) and trimethylchlorosilane (10.8 g, 0.1 mol). The heterogeneous mixture was efficiently stirred at room temperature until it became homogeneous. After removal of hydrogen chloride the residue was distilled with a Vigreux column to give 4.57 g (94%) of the pure siloxane ¹⁸O-**3**; bp $101^{\circ}\text{C}/760\text{ mmHg}$; 21.8% ¹⁸O-content; Lit.⁹ for non-labelled bp $98.5^{\circ}\text{C}/760\text{ mmHg}$.

¹⁸O-methanesulfinyl Chloride ¹⁸O-1

To a mixture of dimethyl disulfide **2** (0.198 g, 2 mmol) and ¹⁸O-hexamethyldisiloxane ¹⁸O-**3** (0.650 g, 4 mmol, ¹⁸O-content 21.8%),

which was cooled to -10°C , sulfuryl chloride (0.81 g, 6 mmol) was added dropwise over a course of 30 min. After completing the addition, the reaction mixture was stirred at this temperature for an additional 30 min and then allowed to reach room temperature over the next 45 min. After removal of the last traces of sulfur dioxide and the whole of the trimethylchlorosilane below room temperature the residue was distilled on a water pump to give pure sulfinyl chloride $^{18}\text{O-1}$; 0.305 g (72%); b.p. $56\text{--}59^{\circ}\text{C}/26\text{ mmHg}$; ^{18}O -content 20.1% (MS assay); $^1\text{H-NMR}$ (CDCl_3) $\delta = 3.37$ (s); Lit.^{4d} for non-labelled b.p. $55^{\circ}\text{C}/40\text{ mmHg}$.

References

1. Patai S, Rappoport Z (eds), *The Chemistry of Sulfinic Acids, Esters and their Derivatives*. Wiley: New York, 1990, chapters 8, 11, 12, 18, 19 and 20.
2. Mikolajczyk M, Drabowicz J, Kielbasinski P. *Chiral Sulfur Reagents; Applications in Asymmetric and Stereoselective Synthesis*, CRC: Boca Raton, 1997.
3. Oae S, Togo H. In *The Chemistry of Sulfinic Acids, Esters and their Derivatives*, Patai S, Rappoport Z (eds). Wiley: New York, 1990, chapter 15.
4. (a) Douglass IB, Farrah BS, Thomas EG. *J Org Chem* 1967; **32**: 3645–3647; (b) Müller W, Schank K. *Chem Ber* 1978; **111**: 2870–2876; (c) Youn IH, Herrman R. *Tetrahedron Lett* 1986; **27**: 1493–1494; (d) Douglass IB, Norton RV *J Org Chem* 1968; **33**: 2104–2106.
5. (a) Drabowicz J, Oae S. *Tetrahedron* 1978; **34**: 63–66; (b) Itoh O, Numata T, Yoshimura T, Oae S. *Bull Chem Soc Jpn* 1983; **56**: 266–269.
6. Drabowicz J, Bujnicki B, Dudzinski B. *Synthetic Commun* 1994; **24**: 1207–1213.
7. Drabowicz J. *Chem Lett* 1981; 1753–1754.
8. Drabowicz J, Bujnicki B, Dudzinski B, Mikolajczyk M. Synthesis of Methanesulfinyl Chloride. PL Patent 169661, April 13, 1993.
9. Sommer LH, Bauman DL. *J Am Chem Soc* 1969; **91**: 7076–7078.